

Angiosarcoma of the liver in Great Britain in proximity to vinyl chloride sites

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Abstract

Objectives—To study the incidence of angiosarcoma of the liver in England and Wales 1979–86 and Scotland 1975–87. To investigate whether any non-occupational neighbourhood cases occurred near a vinyl chloride site.

Methods—This is a geographical study of incident cases among the general population of Great Britain. Diagnosis of angiosarcoma of the liver was based mainly on the national cancer registry, the world register of cases among vinyl chloride workers, and the register of cases (including histological review) maintained by the Health and Safety Executive. Proximity (< 10 km) of residence to a vinyl chloride site was based on postcode of address at the time of diagnosis.

Results—55 cases were ascribed to angiosarcoma of the liver in England and Wales with a further six cases in Scotland (annual incidence in Great Britain from all sources of around 1.4 cases per 10 million population). There were two cases with documented exposure to Thorotrast, and 10 cases among vinyl chloride workers. There were no vinyl chloride sites in Scotland. Among the 25 cases in England and Wales with histological diagnosis after review by a panel of pathologists, only 15 were confirmed as angiosarcoma, and one of the two Scottish cases after histological review was also confirmed. Overall, 11 cases ascribed to angiosarcoma were resident within 10 km of a vinyl chloride site; nine were vinyl chloride workers, one further case on histological review was not considered to have been correctly diagnosed as angiosarcoma, and the remaining case, confirmed as angiosarcoma, was employed at a vinyl chloride factory during the late 1950s, although not as a vinyl chloride worker.

Conclusion—The incidence of angiosarcoma of the liver in Great Britain remains extremely rare. The one confirmed case in a non-vinyl chloride worker within 10 km of a site must nevertheless be presumed to have been exposed to vinyl chloride in the workplace. In the period of study, there were no confirmed non-occupationally exposed cases of angiosarcoma among residents living near a vinyl chloride site in Great Britain.

Keywords: vinyl chloride; angiosarcoma; liver

Angiosarcoma of the liver is an extremely rare, rapidly fatal tumour. An association with occupational exposure to vinyl chloride monomer, used in the manufacture of polyvinyl chloride, was first reported in 1974¹; since then a causal association has been established based on results of human occupational and animal experimental studies.^{2–6} Associations with thorium dioxide (Thorotrast, which until the 1960s was used diagnostically as a radioactive contrast medium) and with arsenic exposure have also been described.^{7–10}

Few studies are available on the incidence of angiosarcoma of the liver among the general population (see Doll¹⁰ for a review). Baxter *et al* reported findings for Great Britain for 1963–73, later extended to 1977, and included one possible non-occupationally exposed neighbourhood case in the vicinity of a vinyl chloride plant.^{7,8} In the present study, we describe the incidence of angiosarcoma of the liver in Great Britain for a later period with multiple sources of information to find possible cases. We were especially concerned with cases resident in the vicinity (within 10 km) of a plant that either handled vinyl chloride or used it for manufacturing. For those cases, we examined whether there was any evidence of occupational exposure to vinyl chloride, Thorotrast, or arsenic, and so whether or not any non-occupational neighbourhood cases had occurred.

Subjects and methods

Information on cases ascribed to angiosarcoma of the liver in Great Britain was sought from five sources (fig 1). Firstly, all cancer registrations coded to 155.0 (primary liver cancer) with histological code 9120 (angiosarcoma) were retrieved from the database of the Small Area Health Statistics Unit.^{11,12} As histological coding for cancer registrations was not introduced until 1979 with the 9th revision of the international classification of disease (ICD-9), data for England and Wales refer to the period 1979–86 (the last year available at the time of study). In Scotland, cancer registrations before 1979 have been recoded to ICD-9, and so data were available for more years (1975–87). The registration details of cases in England and Wales were checked by the former Office of Population Censuses and Surveys (OPCS), and for Scotland by the Information and Statistics Division of the Scottish Health Service.

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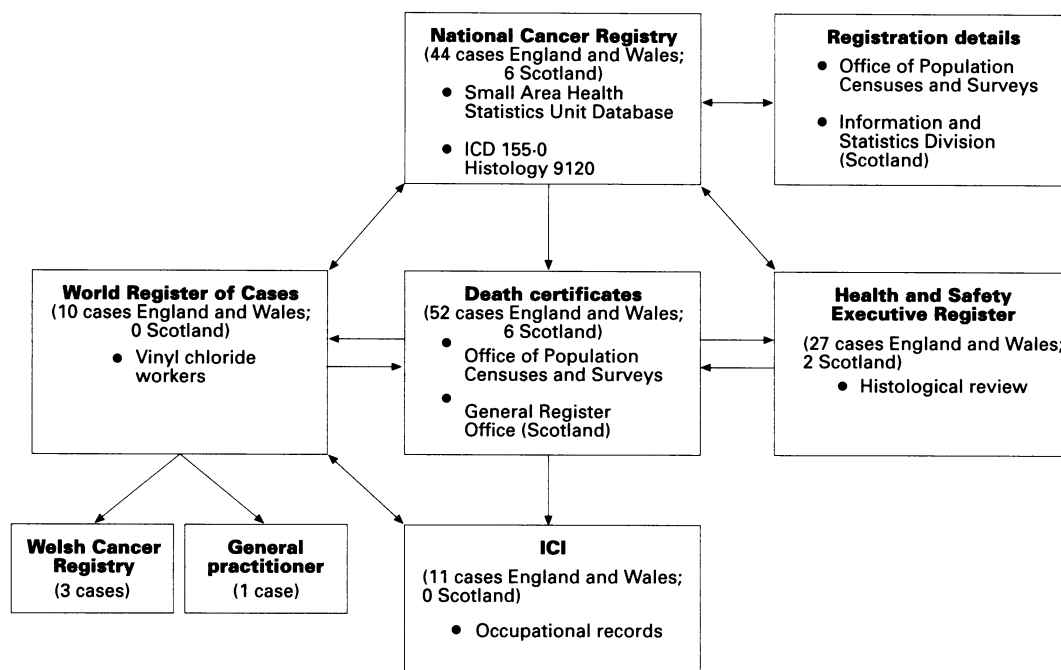
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Figure 1 Sources of cases of angiosarcoma of the liver.



Secondly, copies of death certificates for the incident cases were sought from OPCS for cases in England and Wales and from the General Register Office (Scotland), and both primary and secondary causes of death were ascertained. The death certificates were also examined for mention of occupational exposure to vinyl chloride or industrial disease, and for exposure to Thorotrast or arsenic.

Thirdly, as a further check on cases, the non-confidential parts of the death certificates, including name, sex, address, date of birth, and date of death were abstracted. Extracts from a random sample of death certificates with primary liver cancer as underlying cause of death were included as controls. These were then sent to the Health and Safety Executive for checking against its register of cases, set up in 1974. The register includes histological review by a panel of pathologists of cases identified on the death certificate in Great Britain as angiosarcoma, as well as others identified from published case reports or notes from hospital pathologists or others.⁷ Also, the register was checked for cases presenting with a diagnosis of angiosarcoma of the liver during the period of study that were missing from our lists, and details were sent to us (R Elliott, personal communication). Copies of death certificates (and controls) were also sought for those cases.

Fourthly, extracts of the death certificates for both cases and controls were sent to ICI Chemicals and Polymers to be checked against the occupational records. ICI has responsibility for both its own and former British Petroleum factories, which together contributed around 90% of workers (J Osman, personal communication) to the Health and Safety Executive's Employment Medical Advisory Service study of mortality among all vinyl chloride workers in Great Britain.^{4,13}

Lastly, the United Kingdom entries on the World Register¹⁴ of cases were scrutinised and the details compared with those on the data-

base of the Small Area Health Statistics Unit. Comparison was made of sex, date of birth, date of death, age at diagnosis, and name of factory. We were also able to use the initials of the case (included on the world register) as names were available to us through the death certificates. Information on cases identified from the world register but not traced through the other sources was sought from the Welsh Cancer Registry (three cases) and, where necessary, through the local general practitioner (one case). Copies of death certificates (and controls) not otherwise obtained were retrieved and extracts sent for checking to the other information sources already described.

Information on the 12 vinyl chloride sites in Great Britain was obtained from the Department of the Environment (S Coster, personal communication), to include dates of operation, map grid references, and details of whether vinyl chloride was made, polymerised, used, or stored (fig 2). None of these sites was in Scotland. Cases were located by postcode of residence at the time of the diagnosis of cancer, or death, and the distance from the nearest vinyl chloride site was computed. Postcodes for three of the cases in England and Wales were missing from the database and were obtained from the death certificate or from OPCS.

Results

ENGLAND AND WALES

One duplicate registration was found. Overall, there were 55 cases ascribed to angiosarcoma in England and Wales 1979–86 (53 adults and two children (both female, ages 5 and 6)). Among adults, there were 37 men (ages 36–83 years; median 57 years) and 16 women (ages 25–80; median 59). Numbers of cases a year ranged from three (1986) to 10 (1983) (fig 3).

As expected, there was considerable overlap between sources (table 1). Of the total of 55 cases, 44 were identified on the national can-

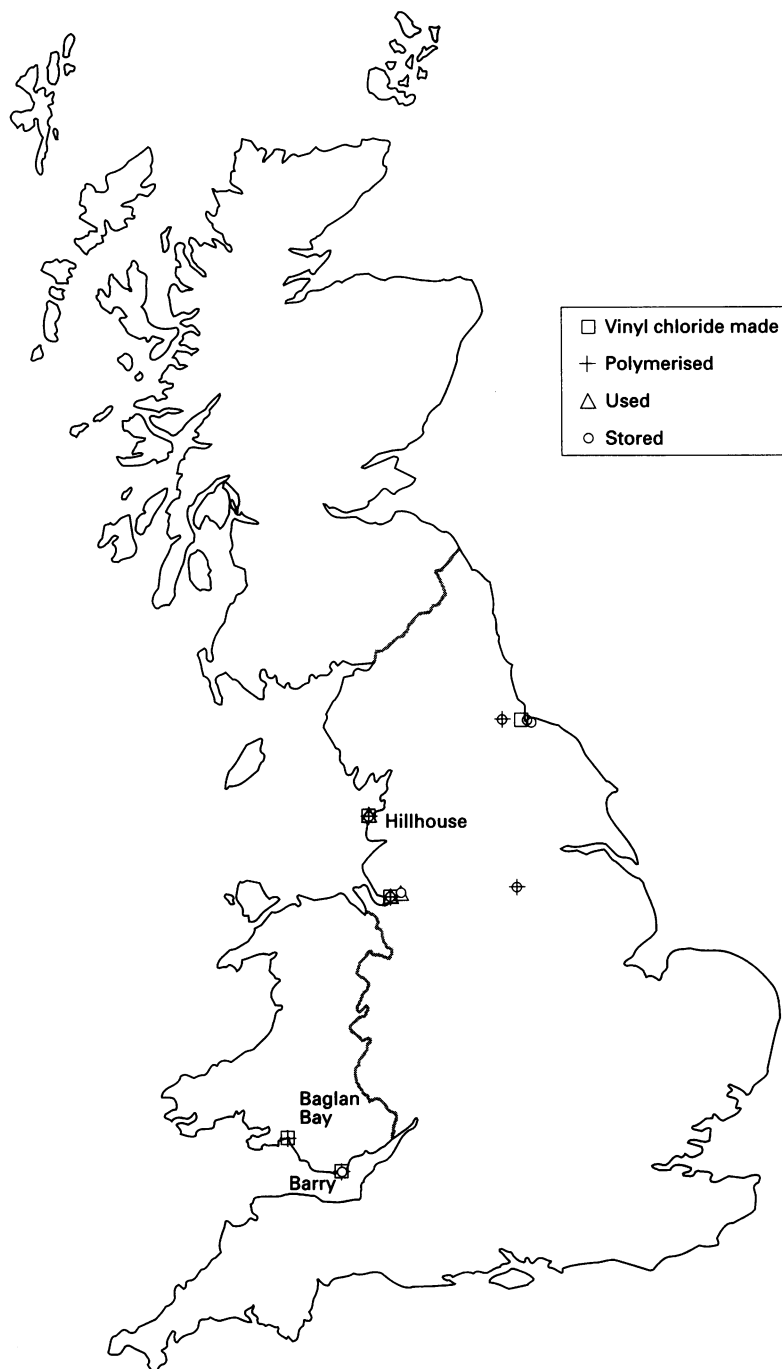
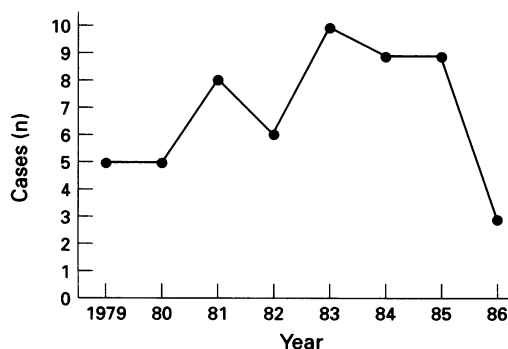


Figure 2 Vinyl chloride sites in Great Britain.

cer registry. Copies of death certificates were obtained for 52 cases including 41 of the 44 cases that were found on the National Cancer Registry, and all 11 identified by ICI from its

Figure 3 Numbers of cases of angiosarcoma of the liver by year, England and Wales, 1979–86.



occupational records, 10 of which also appeared on the World Register for 1979–86. Of these 10 world register cases, only six were also found on the National Cancer Registry, although three further cases were on the Welsh Registry but had not been entered on to the national registry. Nine of the 10 World Register cases were also included among the 27 cases on the Health and Safety Executive register. Seventeen of these 27 cases were on the National Registry, and a further three—that is, nine minus six (table 1, last column)—were on the World Register but not on the National Registry. The remaining seven cases were identified only from the Health and Safety Executive register itself. Two of the 27 cases on the register had pathology recorded as “not yet known”; on panel review of the remaining 25 cases, 15 had the diagnosis of angiosarcoma confirmed (including the case known to ICI that was not on the world register: see discussion of table 2 later), and 10 were considered not to be angiosarcoma.

Death certificate diagnoses of haemangiosarcoma or angiosarcoma of the liver were recorded in 36 of the 52 cases for which a copy of the certificate was obtained, including one as a secondary cause of death, and two that mentioned Thorotrast exposure. Also, three cases were recorded as either haemangioendothelioma (one), haemangioendothelial sarcoma (one), or malignant haemangioma (one), considered to be synonymous with a death certificate diagnosis of angiosarcoma.⁷ One case with a death certificate diagnosis of haemangiocarcinoma and one with carcinomatosis were diagnosed as true angiosarcoma according to the Health and Safety Executive review panel, although the death certificate obtained for the case of carcinomatosis was possibly a mismatch as identifying details included on the register were scanty. One occupational case on the World Register had a death certificate diagnosis of hepatic fibrosis (and industrial disease was noted); the review panel considered that the diagnosis was not angiosarcoma (table 2). Death certificate diagnoses for the remaining 10 cases included hepatic tumour (one); hepatoma (two); chronic liver disease (one); angiocarcinoma of the liver (one); ischaemic heart disease and haemangioma of the liver (one); and four non-hepatic diseases, bronchogenic carcinoma (one), sarcoma of the kidney (one), melanoma (one), and carcinomatosis (one). None of the death certificates mentioned exposure to arsenic.

Table 2 lists all 11 cases in England and Wales ascribed to angiosarcoma during 1979–86 that were resident within 10 km of a vinyl chloride site (fig 2) at the time of the diagnosis of cancer. Nine of these cases were known vinyl chloride workers included on the World Register (the 10th World Register case was resident 11 km from the Barry factory). Eight were also on the Health and Safety Executive register, four with confirmed angiosarcoma, three were considered not to have angiosarcoma, and for one histology was recorded as not yet known.

Table 1 Number of cases by information source, England and Wales, 1979–86 (55 cases in total)

	National Registry*	Death certificate	HSE†	ICI	World Register
National Registry	44	41	17	6	6‡
Death certificate	—	52§	27	11	10
HSE	—	—	27	10	9
ICI	—	—	—	11	10
World Register	—	—	—	—	10

*Primary liver cancer (ICD 155.0) and histology code 9120.

†Health and Safety Executive Register.

‡Three further cases on the World Register were also on the Welsh Cancer Registry (two coded as angiosarcoma of liver) but not on the National Registry.

§Of the 55 cases in total, death certificates were untraceable for three cases on the National Registry.

The total from each source is given along the diagonal; the rows and columns describe the overlap between sources.

The remaining two cases were resident 6 km from a vinyl chloride site (table 2). The first, near the Baglan Bay plant, had no known history of exposure to vinyl chloride and histological review by the panel did not confirm angiosarcoma. The final case was confirmed by ICI as a former employee at the Barry factory, although working as a junior clerk and not a vinyl chloride worker for a period of five months during the late 1950s. The death certificate gave a diagnosis (after necropsy) of angiosarcoma of the liver and noted industrial disease. The Health and Safety Executive register recorded exposure to vinyl chloride and the review panel confirmed the diagnosis of angiosarcoma.

SCOTLAND

Scottish cases were included for consistency with earlier studies.^{7,8} Six cases in Scotland were ascribed to angiosarcoma from 1975–87 (two men, four women); ages ranged from 59 to 81 years. Two cases occurred in 1982; the remainder (one each) in 1976, 1977, 1981, and 1984. Only two of the six cases were included on the Health and Safety Executive register (one confirmed as angiosarcoma on histological review). Death certificate diagnoses included three with haemangiosarcoma or angiosarcoma of the liver (one of which was also on the Health and Safety Executive register with a panel diagnosis considered not to be angiosarcoma). The three other death certificate diagnoses were primary liver cancer (confirmed as angiosarcoma by the review panel),

carcinomatosis of the liver (primary site undetermined), and diffuse poorly differentiated malignant lymphoma. None of the Scottish cases was known to ICI, or appeared on the World Register, and none mentioned Thorotrast or exposure to arsenic.

Discussion

We found 55 cases ascribed to angiosarcoma of the liver in England and Wales, 1979–86 and a further six cases in Scotland, 1975–87 giving a reported annual incidence in Great Britain of around 1.4 cases per 10 million population. These cases were based mainly on cancer registration, the world register of cases and the register maintained by the Health and Safety Executive. There were two cases with documented exposure to Thorotrast, none with exposure to arsenic, and 10 cases occurred in vinyl chloride workers. The incidence of around seven cases a year from all sources is similar to that reported for Great Britain during an earlier period (up to 1977),⁸ although the sources of cases were different. In the previous study,^{7,8} the primary source was death certificates supplemented by case reports and notifications from hospital pathologists and others. Among the 25 (of 27) cases in England and Wales included here from the Health and Safety Executive register with histological review by a panel of pathologists, only 15 were confirmed as angiosarcoma, a higher proportion than in the previous study^{7,8} but based on a smaller percentage of the total number of cases. Only two of the six Scottish cases were included on the Health and Safety Executive register; one was confirmed as angiosarcoma on histological review.

We were particularly concerned in the present study to detect possible neighbourhood (non-occupational) cases in view of the theoretical risk of possible low level environmental hazard related to the operation of vinyl chloride sites, although the historical exposure to high concentrations of vinyl chloride in the workplace has been greatly reduced in recent years.¹⁰ In the previous study in Great Britain, one possible neighbourhood case was described, with no known occupational expo-

Table 2 Angiosarcoma (ASL) cases* within 10 km of a vinyl chloride (VCM) site, England and Wales 1979–86

Site	Year of diagnosis	Age	Sex	Distance from site (km)	Exposure history	World Register	Death certificate	HSE panel diagnosis
Hillhouse	85	48	M	1	VCM	Yes	ASL/Ind	Not ASL
Barry	79	65	M	2	VCM	Yes	ASL/Ind	ASL
Hillhouse	79	58	M	3	VCM	Yes	ASL/Ind	Not ASL
Barry	80	48	M	3	VCM	Yes	ASL/Ind	†
Barry	80	60	M	4	VCM	Yes	§	Not ASL
Barry	81	57	M	5	VCM	Yes	ASL/Ind	ASL
Barry	85	57	M	5	VCM	Yes	ASL/Ind	ASL
Barry	86	37	M	5	VCM	Yes	ASL/Ind	—
Baglan Bay	79	63	M	6	†	No	ASL	Not ASL
Barry	83	42	F	6	‡	No	ASL/Ind	ASL
Barry	84	37	M	8	VCM	Yes	ASL	ASL

*One further occupationally exposed case resident at 11 km.

†Exposure status not known according to HSE register. Case not identified as a worker on ICI records.

‡Recorded as having VCM exposure on HSE register. Worked at Barry plant as junior clerk but not occupationally exposed to VCM according to ICI records.

§Hepatic fibrosis and industrial disease.

¶Histology not yet known according to HSE register. Histology confirmed as angiosarcoma according to World Register.

— = Not on HSE register; HSE = Health and Safety Executive; Ind = industrial disease recorded on death certificate.

sure but residence for six years within half a mile of a plant manufacturing polyvinyl chloride.⁷ In the United States, five non-occupational cases were reported living within a mile of a vinyl chloride plant.⁹ Of these six possible neighbourhood cases, Doll (1988) later excluded two (including the British case) on the grounds that the periods between possible exposure and disease were too short, but concluded that the four other cases were strongly suggestive of an effect of environmental pollution around those plants.

We found 11 cases ascribed to angiosarcoma within 10 km of a vinyl chloride site, eight near the Barry factory, one near Baglan Bay (both in South Wales), and two near Hillhouse (Lancashire). Nine of these cases were vinyl chloride workers, four with confirmed angiosarcoma by review of the panel. Of the two remaining cases, one diagnosis on review was thought not to have been angiosarcoma. The final case with confirmed angiosarcoma, although not a vinyl chloride worker, nevertheless worked at the Barry factory during the late 1950s before the hazards associated with vinyl chloride exposure were known, and before effective containment measures were in place. This case was classed as having an industrial disease; it must be presumed that she had been exposed to vinyl chloride in the workplace. We therefore conclude that, in the period of study, there were no confirmed non-occupationally exposed cases of angiosarcoma among residents living near a vinyl chloride site in Great Britain.

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and for checking registration details of individual cases. We thank OPCS and the General Register Office (Scotland) for providing copies of death certificates. We are grateful for the efforts of the individual cancer registries that submit data to the national cancer registration scheme, and especially the Welsh Cancer Registry for checking cases. We thank S Coster (Department of the Environment), R Elliott, J Osman (Health and Safety Executive), G Paddle, J Paterson, and J Tomenson (ICI Chemicals and Polymers). The views expressed in this publication are those of the authors and not necessarily those of the funding departments.

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